Oral Mesotherapy

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Abstract: Oral mesotherapy is a valuable new option for therapeutic and cosmetic purposes. Its clinical efficiency in the control of various oral diseases has been reported. There are various techniques that were commonly used both inthe dermal and oral mesotherapy. Further researches are recommended to examine the usage of mesotherapy in the different oral conditions.

[Nermin Mohammed Ahmed Yussif and Basma Abd ElAleem El-Saadany. **Oral Mesotherapy.** *Rep Opinion* 2016;8(7):7-12]. ISSN 1553-9873 (print); ISSN 2375-7205 (online). http://www.sciencepub.net/report. 2. doi:10.7537/marsroj08071602.

Key words: Oral mesotherapy, intralesional injection, intraepidermal injection, intramucosal injection, PRP, vitamin D, Vitamin C, hyalouronic acid**.**

1-Introduction

Mesotherapy or local intradermotherapy is a Greek term which describes the type of treatment involving the local delivery of a specific dosage of a drug in the mesoderm layer using micro needles to treat a medical condition or for cosmetic purposes[1, 2].

2-History of mesotherapy

The roots of mesotherapy regards to the 2000 BC in China. In 1952, Dr. Pistor, the father of mesotherapy, has used the intravenous procain for the treatment of a partially deaf patient. The injected procaine was placed in the superficial dermal layer. Perfect results were obtained few hours following the injection. In 1975, the Italian society of mesotherapy (SIM) approved its usage in Italy. In 1980, a group is formed to study the mesotherapy technique and its different applications called CERM. It was followed in 1982 by Pistor who created the international society of mesotherapy. In 1987, the French academy of medicine has recognized mesotherapy as a new specialty[3-5].

3-Theroy behindmesotherapy

The aim behind mesotherpy was to create a new technique favors the supplementation of the needed agents directly and locally to the site of complaint. As previously mentioned, the proposed theory by Pistor depends mainly on the direct effect of the used drug on the tissue originating from mesoderm[4,5].Mesoderm is one of the primary germ layers of the embryo which responsible for the development of skin, connective tissue, muscles, tendons and circulatory system. It is mainly responsible for skin vitality and health[6].The injection technique of mesotherapy depends mainly on the anatomy, histology and dimensions of the tissues. Meso-interface is the horizontal interface between the injected agents and the injected region. For maximum benefits, the injected surface is inversely proportioned to the amount and molecular weight of the injected agent. The wider the meso-interface is, the greater the number of the dermal receptors that activated [7]. On the other hand, the vertical component depends on the depth of penetration. Mesotherapy could be injected either in epidermis, dermis, subcutaneous and regional[4]. The more superficial injection is, the longer the drug remains in the tissue. It permits sustained release of the drug and slow and progressive diffusion into the surrounding tissues [5, 8,9].

4-Techniques ofmesotherapy

There are various techniques of mesotherapy that are different depending on the used needle length and gauge, the injected substance, the depth of penetration and the components of the injected layer. Intraepidermic (IED), nappage, point by point (PPP), mesoperfusion and subcutaneous are the common techniques of mesotherapy[10].

A-Intraepidermic (IED) in which a papule is formed as a result of injection at the epidermis-dermis junction at 1-2 mm depth in which the needle is mostly parallel to the skin. The bevel of the needle usually faces upwards.

B-Nappagein which a deeper injection at 2-4 mm with 30-60 angle is recommended. Two to four injections are recommended with 3-4 mm distance separating each injection and the next point.

C-Point-by-point (PPP) in which a deeper injections at 4 mm depth

D-Mesoperfusion in which injections should be involved at 4-13 mm over 30 to 90 minutes.

For maximum benefits, many rules control the injection procedure. The used needle is called *Lebel needle* in which its bevel is 4 mm long. Its length is determined according to the used technique which ranges between 4-15 mm. fine needles (27-30 gauge). Mesogun is approved from FDA which can either automated or semi-automated[4]. The amount of the injected product is controlled by the Microdeposit theory. It recommends the application of 0.1-0.2 ml per point with 2-3 cm apart. It was found that greater amounts and longer time of the drug to remain in the tissues with shallower penetration. It involves 8-300 injections per the whole treatment sessions. The treatment visits can be spaced either by 1 or 2 weeks. Each session ranges between 3-15 injections[4, 10].

5-Products commonly used in mesotherapy

The drug delivered through skin in dermal mesotherapy has to be hydrophobic and its molecular weight has to be less than 500 Daltons[11]. Mixtures of various agents are commonly used for dermal injections which called Mesococktails. These cocktails are introduced by using the mesogun under local anesthesia[12]. Herbal agents, nutrients, potent vitamins, hormones, enzymes, vasodilators, muscle relaxants, anti-inflammatory, minerals, vaccines, hormones, antibiotics, proteolytic enzymes, anesthetics and anti-oxidants are the main agents used in mesotherapy[4, 13].

The Italian society of mesotherapy (SIM) recommended further protocols to reduce the pain and itching after injection either by dilution of the used agent or the usage of sodium bicarbonate to regulate the pH. The mesococktails contain a vasodilating agent which favors better circulation to the injected site and better uptake of the applied drug. Recently, the usage of mixtures of different agents is not recommended to avoid the side effects of their interactions[5].

The FDA is the association concerning about the assurance of the food and drug safety. However FDA didn't approve the mesotherapy as a technique, it approved many drugs that used in mesotherapy as aminophylline, yohimbine, procaine, lidocaine, marcaine[14] and the delivery method using mesogun[4]. Other drugs didn't have the FDA approval for any purpose of usage as it beyond the scope of FDA because they are not considered drugs as vitamins and minerals[15].

6-Benefits and uses of mesotherapy

The local treatment in mesotherapy has superior advantages over the systemic one either oral or parental. Firstly, it avoids the side effects resulted from drug metabolism and excretion in stomach, intestine, liver and kidneys. Secondly, the effectiveness of the local drug is directly administrated into the area of interest. Finally, it minimizes the dosage used into 1% of the dosage systemically[4].

Improvement of blood flow, removal of fibrotic tissue, increase the connective tissue quality and amount, hair loss (mesohair), skin rejuvenation (mesoglow), excessive fat and cellulite removal, improvement of the lymphatic drainage, osteoarthritis and pain relief are the main medical indications of mesotherapy[16, 17].

7-Complications and criticism of mesotherapy

The main complications reported of this technique include ulceration, bleeding, infections, allergy, abscess, hyperpigmentation and swelling related to the area to be injected[18]. The main problems of mesotherapy are; lack of experience, could not be evaluated except with biopsy and lack of standardized dosage or formulation[4].

8- Oral mesotherapy

Oral mesotherapy is an old technique which was commonly applied in order to introduce various agents. Infiltration, intraligamentary, intramucosal, intralesional and intraepidermic injection are common names for oral mesotherapy technique that have been used previously.

In order to discuss the possible injection modalities that can be used for oral mesotheray, the histological background of the oral tissues should discussed firstly.

Histopathologically, there are great differences between the dermal and oral mesotherapy due to the inherent difference of the injected tissues. The oral cavity is characterized by different type of keratin, the thickness of the epidermal and dermal layers, the presence of lipids, the position of the lipid layer, the amount of blood supply, the amount and the type of the tissue fibers and the rate of tissue renewal[19].

In skin, lipids are mainly found in two main sites; the stratumcorniumand the subcutis layer. On the contrary, the fat distribution in the oral tissues ranges from total absence as in the gingival tissues and maxillary tubrosity into dense fat layer as in palate, retromolar region and buccal mucosa[20]. Therefore, hydrophilic drugs seem to have better absorption characteristics in the oral tissues [11, 21].

9- Common agents delivered by oral mesotherapy

A-local anesthesia

Local anesthesia is a reversible blockage of nerve conduction in a defined area that resulted in loss of sensation[22]. It can be performed by various techniques according to the width of the area needed

to be anesthetized, tissue depth and its relation to nerve. Local infiltrationis one of the techniques in which the local anesthetic solution is administrated submucosal, intradermal or intraligamentary in order to anesthetize the nerve endings that innervatethe required region.The intradermal injection involves introduction of anesthetic agent into the superficial dermis with 10 to 15 degrees and fine needle. While the submucosal injection involves the drug administration in the deep dermis layer reaching the lipid layer with 45 angulations and thicker needle. Field block technique is a type of the submucosal injection which involves the introduction of the anesthetic agentin a circular configuration around the operative site [(23)]. Intraligamentary (periodontal) anesthesia is a type of the locally delivered anesthesia in which the needle is introduced mesiobuccal and distobuccal and the anesthetic agent is pushed in an apical direction. Its accuracy, minimal administration of anesthetic solution and its efficiency in comparison with the other methods with no harmful effects of the adjacent periodontal apparatus are the main advantages of this technique[(24, 25)].

B- Corticosteroids

Corticosteroids used widely for the management of numerous oral inflammatory conditions due to their anti- inflammatory and immune modulator effects.Corticosteroids can be administered intramucosal (within the lesion), topical and systemic[(26)].

Intralesional corticosteroids are the favorable application method, because it delivers the drug directly at the site of required action resulting in rapid action which minimizes its systemic complications. It is commonly used in the management of the longstanding oral lichen planus lesions but, it has a localized side effect such as mucosal atrophy[(27)].

Additionally, intralesional corticosteroid injections considered as a treatment modality for oral submucosal fibrosis which is a chronic debilitating disease of oral mucosa, associated with an increased risk of malignancy[(28)]. Moreover, it was reported in treating mucocele, the surgical approach is the gold standard treatment for treating these lesions. However, some investigators have suggested that the intralesional corticosteroid could be used as new modality in the treatment, but cases of relapse in with corticosteroid have been reported[(29)].

Also, it has been suggested that intralesional steroids injections represent a safe and effective therapy in management of the long-lasting disfiguring enlargement of orofacialgranulomatosis. Great differences were detected in the used doses and the number of sessions according to the severity, extension and the systemic condition of the patient[(28, 30,31)]. However, strong supporting evidence is lacking, due to the variable and inconsistent design of available studies[(32)].

C-Vitamin D

Although the great role of vitamin D in maintaining the bone health and preserving the bone metabolism in an ideal way, it is just recently discovered that vitamin D deficiency has a great role in the occurrence and progression of various periodontal diseases. It is a steroid hormone which controls the bone metabolism and calcium homeostasis. It was detected that the level of vitamin D reaches its lowest levels during periodontal disease especially aggressive periodontitis[(33-35)]. It was reported that its daily supplementation is important for the periodontal health[(36)]. Its usage in orthodontic therapy is considered the commonest usage of vitamin D in dentistry. Small doses are introduced with periodontal injection technique. It depends on accelerating the osteoclastic activity which in role accelerates the orthodontic movement. The dose and the number of the treatment sessions are determined according to the distance that the tooth needed to travel [(37,38)].

D-Platelet-rich plasma (PRP)

Platelet-rich plasma (PRP) is defined as a portion of the plasma element of autologous blood having a platelet concentration above baseline[(39, 40)].

PRP considered as a growth factor agonist[(41)] and has both mitogenic and chemotactic properties[(39)]. It contains a high level of platelets and a full supplement of clotting and growth factors[(40)].

It was found that intralesional injection is a newly described method for application of PRP and represents an effective therapeutic option when dealing with non healing wounds[(42)]. These findings open the door in front of using intralesional PRP in oral chronic ulcers. In 2015, improvement in pain threshold, better ability to eat and a reduction in pemphigus disease were reported. The PRP injections seems to accelerate the healing process and decrease the pain and eating discomfort associated with the oral lesions of [(43)]. Further randomized clinical trials should be conducted to assess the efficacy and safety of PRP use in PV and other chronic resistant oral ulcerations.

D- Vitamin C

Ascorbic acid is also an essential vitamin in the treatment of periodontal diseases. Its deficiency causes impaired wound healing and higher bleeding tendency. It is a scavenging powerful anti-oxidant. It also has a great role in collagen bio-synthesis[(44)]. High expression of collagenase-1 in maintaining the extracellular matrix turns over. Vitamin C is usually

accumulated in the immune cells as PMNs and macrophages. It significantly enhances chemotaxis, phagocytic, opsonization, degranulation and killing functions of immune cells. Lower levels of serum vitamin C were detected in periodotitis[36, 45]. It is widely used in dermal mesotherapy as it restores the microcirculation by neutralizing the free radicals in the newly formed tissues, stimulate the collagen formation and inhibit melanogenesis[16, 46]. It could be supplied orally, topically or by intraepidermic injection[47, 48]. Recently, it was locally injected using intraepidermic technique in order to restore the gingival health and reduce its hyperpigementation. Minimal doses also stimulate collagen formation and better vasculature[48].

E-Hyalouronic acid

Hyalouronic acid is an important component of the extracellular matrix which has great role in maintaining the health of the oral tissues and repair process. The mechanism of its action depends mainly on stimulating the cellular proliferation, migration, vasculature and restoring the integrity of epidermal and dermal layer. It is also effective in stimulation the collagen formation through enhancement the proliferation of fibroblasts. In dentistry, it is recently used to accelerate the healing of oral ulcers[49], extraction socket[50] and gingival inflammation[51] either through injection or topical application. It was also used in reconstruction of the interdental papilla instead of the conventional surgical intervention[52, 53].

Conclusion

The bidirectional relationship between oral and systemic condition make it difficult to provide a safe treatment that can achieve favorable treatment with minimal side effects. Nowadays, mesotherapy becomes more necessary in dentistry to overcome the huge number of surgical interventions either for therapeutic or cosmetic purposes. It also limits the need for systemic drugs which provides dealing with the systemic diseases in a better way. Further researches are needed to examine the usage of mesotherapy in the different oral complaints.

References

1. Morganti P., Fabrizi G. and James B.: An innovative cosmeceutical with skin whitening activity. Journal of Applied Cosmetology, 17 (4): 144-53, 1999.
2. Le Coz J.: History of mesotherapy. Am J Mesother., 3: 16-18, 2009.
3. Pistor M.: What is mesotherapy? Chir Dent Fr., 46: 9-60, 1976.
4. Materasso A., Pfeifar T.:Mesotherapy for Body contouring. PlastReconstr Surg., 115, 1420-1424, 2005.Achar S., Kundu S.: Principles of office anesthesia: part I. Infiltrative anesthesia. AmFamPhys, 66(1):91-4, 2002.
5. Mammucari M., Gatti A., Maggiori S., Bartoletti C.,Sabato A.: Mesotherapy, definition, rationale and clinical role: a consensus report from the Italian Society of Mesotherapy. European Review for Medical and Pharmacological Sciences, 15: 682-694, 2011.
6. Adelson H.: French Mesotherapy for the Treatment of Pain. Am J Meso, 4: 21–23.2, 2006.
7. Herreros F., de Moraes A., Velho P.: Mesotherapy: a bibliographical review. Anais Brasileiros Dermatologia, 86(1):96-101, 2011.
8. Binaglia L., Marconi P., Pitzurra M.: The diffusion of intradermally administered procaine. J Mesother., 1: 15-28, 1981.
9. American Society of Plastic Surgeons (ASPS) guiding principles for mesotherapy, 7 (8), 2008.
10. Latha P., Vandana K.: Mesotherapy – a review. International Journal of Advanced Pharmaceutics, 1 (1): 19-29, 2011.
11. Bos J., Meinardi M.: The 500 Dalton rule for the skin penetration of chemical compounds and drugs. Exp Dermatol., 9(3):165–9, 2000.
12. Rohrich R.:Mesotherapy what is it? Does it work? PlastReconstr Surg., 115: 1425, 2005.
13. Savoia A., Landi S., Baldi A.: A New Minimally Invasive Mesotherapy Technique for Facial Rejuvenation. Dermatol Ther (Heidelb), 3:83–93, 2013.
14. Menkes C., Laoussadi S., Kac-Ohana N., Lasserre O.: Controlled trial of Injectable Diclofenac in Mesotherapy for the Treatment of Tendinitis. Bulletin SFM,4, 250-252, 2002.
15. Palermo S. et al.: Mesotherapy Association in the therapy of cervicobrachialgia. Minerva Anesiol., 57, 1084-1085, 1991.
16. Bryant R.: Controversial mesotherapy. Derm Times., 25(1), 2004.
17. Donofrio L.: Mesotherapy. Cosm Derm, 20 (2): 97-98, 2007.
18. Conforti G., Capone L., Corra S.: Intradermal Therapy (Mesotherapy) for the Treatment of Acute Pain in Carpal Tunnel Syndrome: A Preliminary Study. Korean J Pain, 27(1): 49-53, 2014.
19. Nanci A., Bosshardt D.: Structure of periodontal tissues in health and disease. Periodontology 2000, 40: 11–28, 2006.
20. Zuhr O., Baumer D., Heurzeler M.: The addition of soft tissue replacement grafts inplastic periodontal and implant surgery: critical elements in design and execution. J Clin Periodontol., 41 (15): 123–142, 2014.
21. Prausnitz M., Mitragotri S., Langer R.: Current status and future potential of transdermal drug

delivery. Nat Rev Drug Discov., 3(2):115–24, 2004.
22. Achar S., Kundu S.: Principles of office anesthesia: part I. Infiltrative anesthesia. Am Fam Physician, 66(1):91-4, 2002.
23. McGee D.: Local and topical anesthesia. Roberts JR, Hedges J. Clinical procedures in emergency medicine. 4th ed. Philadelphia, Pa: WB Saunders; 533-51, 2004.
24. Tsirlis A., Iakovidis D., Parisis N.: Dry socket: frequency of occurrence after intraligamentary anesthesia. Quintessence Int., 23(8):575–7, 1992.
25. Meechan J., Thomason J.: Acomparison of 2 topical anesthetics on the discomfort of intraligamentary injections: a double-blind, split-mouthvolunteers clinical trial. Oral Surg Oral Med Oral Pathol Oral Radiol Endod.,87(3): 62-5, 1999.
26. Masthan K., Aravindha Babu N., Jha A., Elumalai M.: Steroids application in oral diseases. Int. J. Pharma Bio Sci., 4, 829–834, 2013.
27. Xia J., Li C., Hong Y., Yang L., Huang Y., Cheng B.: Short- term clinical evaluation of intralesional triamcinolone acetonide injection for ulcerative oral planus. J Oral Pathol Med., 35: 327-31, 2006.
28. Singh M., Niranjan H., Mehrotra R., Sharma D., Gupta S.: Efficacy of hydrocortisone acetate / hyaluronidase vs triamcinolone acetonide / hyaluronidase in the treatment of oral submucous fibrosis. Indian J Med Res., 131, 665-669, 2010.
29. Baharvand M., Sabounchi S., Mortazavi H.: Treatment of Labial Mucocele by Intralesional Injection of Dexamethasone : Case Ser., 3, 128–133, 2014.
30. Schlosser B.: Lichen planus and lichenoid reactions of the oral mucosa. Derma Ther., 23, 251–267, 2010.
31. Da Silva Júnior., Carreira S., Pedreira E., Tuji F., Ortega K., Pinheiro J.: Treatment of central giant cell lesions using bisphosphonates with intralesional corticosteroid injections. Head & Face Med., 8:23, 2012.
32. Fedele S., Fung P., Bamashmous N., Petrie A., Porter S.: Long-term effectiveness of intralesional triamcinolone acetonide therapy in orofacial granulomatosis : an observational cohort study, Br J Dermatol.794–801, 2014.
33. Amano Y., Komiyama K., Makishima M.: Vitamin D and periodontal disease. J Oral Sci., 51(1): 11-20, 2009.
34. Liu K., Meng H., Lu R., Xu L., Zhang L., Chen Z., Shi D., Feng X., Tang X.: Initial periodontal therapy reduced systemic and local 25-hydroxy vitamin D3 and interleukin-1b in patients with aggressive periodontitis. J Periodontol.,81: 260-266, 2010.
35. Zhang X., Meng H., Xu L., Zhang L., Shi D., Feng X., Lu R., Chen Z.: Vitamin D-binding protein levels in plasma and gingival crevicular fluid of patients with generalized aggressive periodontitis. Int J Endocrinol., 1-6, 2014.
36. Van der Velden U., Kuzmanova D., Chapple I.: Micronutritional approaches toperiodontal therapy. J ClinPeriodontol., 38 (11): 142–158, 2011.
37. Collins M., Sinclair P.: The local use- of vitamin D to increase the rate of orthodontic tooth movement. J Ortho Dentofac Orthop., 94:278-84, 1988.
38. Al-Hasani N., AL-Bustani A., Ghareeb M., Hussain S.: Clinical efficacy of locally injected calcitriol in orthodontic tooth movement. International Journal of Pharmacy and Pharmaceutical Sciences, 3 (5), 2011.
39. Marx R.: Platelet-rich plasma (PRP): what is PRP and what is not PRP? Implant Dent. 10, 225–8, 2001.
40. Mehta S., Watson J.: Platelet Rich Concentrate: Basic Science and Current Clinical Applications. J. Orthop. Trauma, 22, 432–438, 2008.
41. Petrova N., Edmonds M.: Emerging drugs for diabetic foot ulcers. Expert Opin. Emerg. Drugs 11, 709–24, 2006.
42. D43- El-Komy M., Hassan A., Raheem H., Doss S., El-Kaliouby M., Saleh N., Saleh M.:Platelet-rich plasma for resistant oral erosions of pemphigus vulgaris: A pilot study. Wound Repair Regen. 23, 953–955, 2015.
43. Padayatty S., Katz A., Wang Y., Eck P., Kwon O., Lee J., Chen S., Corpe S., Dutta A., Dutta S., Levine M.: Vitamin C as an antioxidant: evaluation of its role in disease prevention. Journal of the American College of Nutrition, 22 (1): 18–35, 2003.
44. Kuzmanova D., Jansen I., Schoenmaker T., Nazmi K., Teeuw W., Bizzarro S., Loos B.,Velden van der U.: Vitamin C in plasma and leucocytes in relation to periodontitis. J Clin Periodont, 39: 905–912, 2012.
45. Chase C.: Common complications and Adverse Reactions. Bulletin SFM,10 (8): 2005.
46. Shimada Y., Tai H., Tanaka A., Ikezawa-Suzuki I., Takagi K., Yoshida Y. and Yoshie H.: Effects of ascorbic acid on gingival melanin pigmentation in vitro and in vivo. J of Periodont., 80:317-323, 2009.
47. Yussif N., Zayed S., Hasan S., Sadek S.: Evaluation of injectable Vitamin C as a depigmenting agent in physiologic gingival

melanin hyperpigmentation: A clinical trial. Rep Opinion 2016;8(6):113-120.
48. Nolon A., Baillie C., Badminton J., Rudralinglam M., Seymour R.: The efficacy of topical hyaluronic acid inthe management of recurrent aphthous ulceration. J Oral Pathol Med., 35(8):461-5, 2006.
49. Mendes R., Silva G., Lima M., Calliari M., Almeida A., Alves J., et al.: Sodium hyaluronate accelerates the healing process in tooth sockets of rats. Arch Oral Biol., 53(12):1155-62, 2008.
50. Jentsch H., Pomowski R., Kundt G., Göcke R.: Treatment of gingivitis with hyaluronan, J Clin Periodontal., 30(2):159-64, 2003.
51. Becker W., Gabitov I., Stepanov M., Kois J., Smidt A., Becker B.: Minimally invasive treatment for papillae deficiencies in the esthetic zone: a pilot study Clinical Imp Dent &Rel Res., 12 (1), 2010.
52. Mansouri S., Ghasemi M., Salmani Z., Shams N.: Clinical application of hyaluronic acid gel for reconstruction of interdental papilla at the esthetic zone. J Islam Den Assoc IRAN, 25, (2), 152-157, 2013.

6/26/2016